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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,557	08/25/2000	Christian Devaux	1017753-000152	5736
21839 7590 03/24/2009 BUCHANAN, INGERSOLL & ROONEY PC POST OFFICE BOX 1404 ALEXANDRIA, VA 22313-1404			EXAMINER PARKIN, JEFFREY S	
			ART UNIT 1648	PAPER NUMBER
			NOTIFICATION DATE 03/24/2009	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No. 09/648,557	Applicant(s) DEVAUX ET AL.	
	Examiner Jeffrey S. Parkin	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-42 and 45-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-42 and 45-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment submitted 19 December, 2007. Claims 31-42 and 45-53 are pending in the instant application.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claim references a complex comprising "about 20 molecules" of MPG per molecule of antiviral peptide. This phrase is a relative term that does not allow the skilled artisan to quantify the actual number of MPG molecules present. For instance, do 15 or 16 or 17 or 18 or 19 or 21 or 22 or 23 or 24 or 25 MPG molecules comprise "about 20"? Appropriate

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correction is required (e.g., simply reciting 20 molecules of MPG would obviate the rejection).

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The previous rejection of claims 31-53 under 35 U.S.C. § 103(a) as being unpatentable over Morris *et al.* (1999) in view of Korber *et al.* (1998), is hereby withdrawn in response to applicants' amendment and the declaration previously provided (see the communication filed 19 December, 2007).

Claims 31-38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Divita *et al.* (1995) in view of Bolognesi *et al.* (1995) and Korber *et al.* (1998). The claims are drawn toward a decameric antiviral polypeptide consisting of the following structure: $\text{NH}_2\text{-[K/R]}_1\text{[D/E]}_2\text{[VIT]}_3\text{W[D/E]}_5\text{[A/T/Q]}_6\text{WW[A/V/I/T/M/D]}_9\text{[D/E/N]}_{10}\text{-COOH}$. The decapeptide must be capable of inhibiting the dimerization of HIV RT and not consist of SEQ ID NO.: 1 (KETWETWWTE). Claims 32-34 recite various permissible amino acid substitutions. Claim 35 includes a pharmaceutically-acceptable excipient. Claims 36-38 encompass a carrier (e.g., liposome,

protein, microparticle, peptide, etc.) that facilitates entry of the peptide into the cell.

Devita et al. (1997) prepared a synthetic 19-mer (P1-FKLPIQKETWETWWTEYWE) corresponding to the tryptophan-rich repeat motif that is required for the dimerization of HIV-1 and -2 RTs (see p. 28643, EXPERIMENTAL PROCEDURES, *Materials*). This peptide was a potent inhibitor of the dimerization process in both RTs (see Table I, p. 28643; Fig. 1, p. 28644). The authors concluded (see p. 28642, Abstract) that "the same peptide can also inhibit human immunodeficiency virus type 2 reverse transcriptase dimerization, suggesting the same inhibitors might be used as agents against both viruses as well as against variants of human immunodeficiency virus type 1 that differ from the variant against which they were developed." This teaching does not disclose decameric peptide inhibitors of RT.

Bolognesi et al. (1995) designed a number of 36-mer synthetic peptide inhibitors of HIV-1 cell fusion. The parent peptides correspond to amino acids 638-673 of gp41 from several different HIV-1 (e.g., LAI, SF2, RF, MN) and -2 isolates (e.g., ROD, NIHZ). The authors performed detailed peptide mapping studies to identify the most potent inhibitors. Specifically, amino- and carboxyl-truncations were generated (see Table I, cols. 5 and 6, and Table II, col. 6, respectively). The shortest truncations contained as few as three amino acids. A detailed discussion about the generation of inhibitory analogues through one or more amino acid substitutions was also provided (see cols. 7 and 8). This would prove useful in the generation of fusion inhibitors against other viral isolates, as well as, the generation of

peptides with advantageous features (e.g., increased bioavailability). Finally, it was reported that various carriers (e.g., see col. 10) could be attached to the peptides. This teaching does not disclose decameric RT inhibitors.

Korber *et al.* (1998) provide the complete amino acid sequence of RT from a number of HIV-1, -2, and SIV isolates (see p. II-A-16). The Los Alamos database contains over 30,000 different sequence listings. This teaching does not disclose decameric RT inhibitors.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to subject the 19-mer peptide RT inhibitors of Devita *et al.* (1997), to further analysis as provided by Bolognesi *et al.* (1995), since this would facilitate the identification of the minimal peptide required for antiviral activity. One of ordinary skill in the art would have been motivated to make a shorter peptide for obvious economic reasons. Moreover, employing the various RT amino acid sequences provided by Korber *et al.* (1998), one of ordinary skill in the art would have been motivated to prepare additional sequences from other isolates to facilitate the development of antivirals against those isolates and for the development of a broad spectrum antiviral. One of ordinary skill in the art would have had a reasonable expectation of success because they would be choosing from a limited number of predictable solutions. The parent P1 peptide was only 19 amino acids in length. One of ordinary skill in the art employing the methods of Bolognesi and colleagues could readily prepare a small number of amino- and carboxyl-

truncations and screen them for their inhibitory activity to identify the claimed decameric peptide. All that is required to arrive at the claimed invention is routine experimentation.

Claims 39-42 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Divita *et al.* (1995) in view of Bolognesi *et al.* (1997) and Korber *et al.* (1998), as applied *supra* to claims 31-38, and further in view of Morris *et al.* (1997). The claims are directed toward a decameric polypeptide comprising an MPG peptidyl carrier. Morris and colleagues provide a carrier (e.g., MPG) that is useful for transporting molecules across the cell membrane and delivering them to the cytoplasm or nucleus (see p. 2730, Abstract). The authors provide the complete amino acid sequence (GALFLGFLGAAGSTMGAWSQPKSKRKV) of this carrier. Structural details concerning each domain of the MPG carrier were also provided. The N-terminal domain contains 17 residues (GALFLGFLGAAGSTMGA) from the fusion region of HIV-1 gp41 and the C-terminal domain contains an SV40 large T antigen nuclear localization signal (NLS). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ an MPG carrier, as provided by Morris *et al.* (1997), to transport antiviral peptides across the cell membrane to facilitate their antiviral activity.

Claims 45-53 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Divita *et al.* (1995) in view of Bolognesi *et al.* (1997), Korber *et al.* (1998), and Morris *et al.* (1997). The claims are drawn toward a chimeric protein comprising a decameric antiviral polypeptide consisting of the following structure: NH₂-[K/R]₁[D/E]₂[VIT]₃W[D/E]₅[A/T/Q]₆WW[A/V/I/T/M/D]₉

[D/E/N]₁₀-COOH and an MPG carrier. The chimeric peptide must be capable of inhibiting the dimerization of HIV RT. Claims 46-48 and 51 recite various permissible amino acid substitutions. Claim 49 includes a pharmaceutically-acceptable excipient. Claims 50, 52, and 53 encompass a carriers or chimeras with the recited sequences.

Devita et al. (1997) prepared a synthetic 19-mer (P1-FKLPIQKETWETWWTEYWE) corresponding to the tryptophan-rich repeat motif that is required for the dimerization of HIV-1 and -2 RTs (see p. 28643, EXPERIMENTAL PROCEDURES, *Materials*). This peptide was a potent inhibitor of the dimerization process in both RTs (see Table I, p. 28643; Fig. 1, p. 28644). The authors concluded (see p. 28642, Abstract) that "the same peptide can also inhibit human immunodeficiency virus type 2 reverse transcriptase dimerization, suggesting the same inhibitors might be used as agents against both viruses as well as against variants of human immunodeficiency virus type 1 that differ from the variant against which they were developed." This teaching does not disclose decameric peptide inhibitors of RT.

Bolognesi et al. (1995) designed a number of 36-mer synthetic peptide inhibitors of HIV-1 cell fusion. The parent peptides correspond to amino acids 638-673 of gp41 from several different HIV-1 (e.g., LAI, SF2, RF, MN) and -2 isolates (e.g., ROD, NIHZ). The authors performed detailed peptide mapping studies to identify the most potent inhibitors. Specifically, amino- and carboxyl-truncations were generated (see Table I, cols. 5 and 6, and Table II, col. 6, respectively). The shortest truncations contained as few as three amino acids. A detailed discussion

about the generation of inhibitory analogues through one or more amino acid substitutions was also provided (see cols. 7 and 8). This would prove useful in the generation of fusion inhibitors against other viral isolates, as well as, the generation of peptides with advantageous features (e.g., increased bioavailability). Finally, it was reported that various carriers (e.g., see col. 10) could be attached to the peptides. This teaching does not disclose decameric RT inhibitors.

Korber *et al.* (1998) provide the complete amino acid sequence of RT from a number of HIV-1, -2, and SIV isolates (see p. II-A-16). The Los Alamos database contains over 30,000 different sequence listings. This teaching does not disclose decameric RT inhibitors.

Morris and colleagues provide a carrier (e.g., MPG) that is useful for transporting molecules across the cell membrane and delivering them to the cytoplasm or nucleus (see p. 2730, Abstract). The authors provide the complete amino acid sequence (GALFLGFLGAAGSTMGAWSQPKSKRKV) of this carrier. Structural details concerning each domain of the MPG carrier were also provided. The N-terminal domain contains 17 residues (GALFLGFLGAAGSTMGA) from the fusion region of HIV-1 gp41 and the C-terminal domain contains an SV40 large T antigen nuclear localization signal (NLS).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to subject the 19-mer peptide RT inhibitors of Devita *et al.* (1997), to further analysis as provided by Bolognesi *et al.*

(1995), since this would facilitate the identification of the minimal peptide required for antiviral activity. One of ordinary skill in the art would have been motivated to make a shorter peptide for obvious economic reasons. Moreover, employing the various RT amino acid sequences provided by Korber *et al.* (1998), one of ordinary skill in the art would have been motivated to prepare additional sequences from other isolates to facilitate the development of antivirals against those isolates and for the development of a broad spectrum antiviral. One of ordinary skill in the art would have had a reasonable expectation of success because they would be choosing from a limited number of predictable solutions. The parent P1 peptide was only 19 amino acids in length. One of ordinary skill in the art employing the methods of Bolognesi and colleagues could readily prepare a small number of amino- and carboxyl-truncations and screen them for their inhibitory activity to identify the claimed decameric peptide. All that is required to arrive at the claimed invention is routine experimentation. Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ an MPG carrier, as provided by Morris *et al.* (1997), to transport antiviral peptides across the cell membrane to facilitate their antiviral activity. One of ordinary skill in the art would have been motivated to use the full-length MPG amino acid sequence (SEQ ID NO.:2), as well as, truncated variants of this sequence (SEQ ID NOS.: 4 and 6), to deliver antivirals to the cell.

Additional Prior Art

- van der Burg, S. H., et al., 1997, HIV-1 reverse transcriptase-specific CTL against conserved epitopes do not protect against progression to AIDS, J. Immunol. 159:3648-3654. This article describes a CTL epitope mapping study performed on the HIV-1 RT. Overlapping decamers of the entire RT were generated including the sequence KETWETWWTE which corresponds to SEQ ID NO.: 1 (see Fig. 3, p. 3652, panel C, tp 1). Although this study did not address the antiviral properties of this peptide per se, nevertheless it was identical to that previously encompassed by the claim language and would be expected to display the same biological properties (see applicants' response filed 19 December, 2007).

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information

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Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

17 March, 2009